

B. V. Rama Sastry, D.Sc., Ph.D.  
Professor of Pharmacology  
Vanderbilt University School of Medicine  
Nashville, Tennessee 37232

Influence of Nicotine on the Release of Acetylcholine in the Human Placenta  
and its Implications on the Fetal Growth.

As a part of this project, the existence of a unique cholinergic system in human placenta was demonstrated. This system contains acetylcholine (ACh), choline acetyltransferase (ChA, the enzyme that catalyzes the synthesis of ACh from acetylcoenzyme A and choline) and acetylcholinesterase (AChE, the enzyme that hydrolyzes ACh into acetate and choline). This ACh-ChA-AChE system is unique because there is no evidence for the presence of nerves in the human placenta. Moreover, it is localized in the syncytiotrophoblast, a cell layer which separates the maternal circulation from fetal circulation.

Nicotine showed a biphasic effect on the rate of ACh release from the isolated placental villus. Thus: at  $5.8 \times 10^{-6}$  M of nicotine there was no effect; at  $5.8 \times 10^{-5}$  M of nicotine the rate of ACh release increased by about 40%; and at  $7.7 \times 10^{-4}$  M the rate was depressed by about 30%. The stimulatory effect of nicotine was depressed significantly by atropine, but not by d-tubocurarine. It was suggested that the release of ACh by nicotine was probably mediated through a cholinergic receptor of the muscarinic type.

The future studies will be aimed at (a) the mechanisms of ACh release by nicotine from placenta, (b) the effects of carbon monoxide and anoxia on the ACh release, uptake of nutrients (amino acids and sugars) by the placental villus, and (c) the effects of anoxia on the lactic acid production which in turn may participate in the formation of lactoyl-CoA and lactoylcholine ("a false local hormone?")

Activation Date: May 1, 1976

Current Grant Level: \$16,892.

1005075560